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continued 2 to 3 days postoperatively. In the recovery room, morphine sulfate 2 mg IV or meperidine 12.5 mg IV is a reasonable starting dose for an opioid-naive 70-kg patient. The dose may have to be repeated at short intervals (eg, q 15 to 30 min) until pain relief is established. On the ward, parenteral morphine sulfate 8 to 10 mg q 3 h usually provides pain relief. Higher doses provide greater analgesia and a longer duration of effect. Patient-controlled analgesia allows self-administration of small opioid doses as needed.

Dosage should be modified according to the patient's response. The need for individualized dosing postoperatively was the major impetus for developing patient-controlled analgesia techniques.

CANCER PAIN

Cancer pain syndromes may be caused by tumors invading bone or soft tissues, compressing or infiltrating nerves or blood vessels, or obstructing a hollow viscus, or they may follow surgery, chemotherapy, or radiation therapy. Accurate diagnosis of the underlying process is essential because specific treatment can simplify pain management. However, pain should be adequately treated while its cause is being sought.

Nonopioid analgesics may be used when pain is mild to moderate (see TABLE 167–1). Opioids are often used with nonopioids, as a combination drug (usually propoxyphene, codeine, or oxycodone combined with aspirin or acetaminophen) or as two drugs taken together. The drugs are given around the clock until the maximum safe dose of the nonopioid drug is reached (eg, 12 tablets of acetaminophen 325 mg and oxycodone 5 mg per day). If this dosage is inadequate, a combination drug should not be used; the nonopioid may be continued at the maximum safe dose, and an opioid given at whatever dose is needed. Meperidine is not recommended because of its CNS adverse effects. Agonist-antagonist drugs play a limited role because they have a ceiling dose for analgesia and because they may induce an acute abstinence syndrome in patients physically dependent on opioids.

Bone pain appears to be particularly responsive to NSAIDs, which may be given with an opioid. Many other drugs whose primary indication is not analgesia (so-called adjuvant analgesics) can augment pain relief in certain settings; corticosteroids (eg, dexamethasone 4 mg or more po q 6 h) are effective for severe bone pain and may be effective for pain due to infiltration of neural structures.

NEUROPATHIC PAIN

Chronic pain can develop after injury to any level of the nervous system, peripheral or central. A variety of specific syndromes have been identified. Their pathogenesis is obscure, and their incidence and prevalence are unknown but appear to be low relative to the injuries that precede them, except for root avulsion injuries and phantom limb pain.

The sustaining mechanisms of two broad categories of neuropathic pain appear to involve reorganization of central somatosensory processing: **deafferentation pain** (due to partial or complete interruption of peripheral or central afferent neural activity) and **sympathetically maintained pain** (dependent on efferent sympathetic activity). Both are complex, and although presumably related pathogenetically, they differ substantially. For example, a thalamic lesion that causes pain without autonomic or trophic changes and that is unresponsive to manipulation of the sympathetic nervous system is clearly distinct from a lesion that produces reflex sympathetic dystrophy, in which all of these characteristics may be present. Deafferentation pain syndromes include postherpetic neuralgia, central pain (pain after CNS injury), and phantom pain. Phantom pain is experienced in the region of the missing body part after any type of amputation; phantom limb pain is the best characterized type.

Neuropathic pain may involve predominantly **peripheral processes**; peripheral syndromes include neuroma formation and nerve compression (eg, radiculopathy from discogenic disease). In addition to the measures described below, primary therapies directed at the peripheral focus (eg, nerve decompression) may help.

Although neuropathic pain may produce deep aching, dysesthesias, such as spontaneous or evoked burning pain, often with a superimposed lancinating component, may occur and are more diagnostic. Other sen-

sations—eg, hyperesthesia, hyperalgesia, allodynia (pain from a non-noxious stimulus), and hyperpathia (particularly unpleasant, exaggerated pain response)—may also occur.

Diagnosis and Treatment

Accurate diagnosis is essential. Deafferentation pain due to peripheral nerve damage must be distinguished from other forms of neuropathic pain in which an ongoing, potentially treatable pathologic process affects a peripheral nerve. Pain that may be ameliorated by manipulating the sympathetic nervous system (ie, sympathetically maintained pain) should be distinguished from pain that is not.

Treatment applied without concern for diagnosis, rehabilitation, and psychosocial issues has a limited chance of success. Mobilization is important with peripheral nerve lesions to prevent trophic changes, disuse atrophy, and joint ankylosis. Psychologic factors must be constantly considered from the start of therapy. Anxiety and depression must be treated appropriately. When dysfunction is entrenched, patients may benefit from the comprehensive approach provided by a pain clinic.

Neuropathic pain syndromes, except for the complex regional pain syndrome, usually do not respond to sympathetic blockade. These syndromes include postherpetic neuralgia (see HERPES ZOSTER in Ch. 162), phantom limb pain, root avulsions, painful traumatic mononeuropathy, painful polyneuropathy, central pain syndromes (potentially caused by virtually any lesion at any level of the nervous system), and postsurgical pain syndromes (eg, postmastectomy syndrome, postthoracotomy syndrome, stump pain). For these syndromes, all nondrug therapies (see COMPLEX REGIONAL PAIN SYNDROME, below) except sympathetic blockade may be tried.

A tricyclic antidepressant (eg, amitriptyline or desipramine 10 to 25 mg po at bedtime, increasing to 75 to 150 mg over 1 to 2 wk) may be useful. Higher doses may be needed, especially if depression is prominent. A lancinating component of neuropathic pain may respond to an anticonvulsant or to baclofen. Doses of these drugs (except phenytoin) should be low initially and increased gradually; usual doses are baclofen 10 to 80 mg/day, carbamazepine 200 to 1200 mg/day, clonazepam 1 to 10 mg/day, and valproate 750 to 2250 mg/day. Phenytoin should be started at the usual maintenance dose (eg, 300 mg/day po) or given first as a loading dose (eg, 500 mg po q 6 h for two doses, then 300 mg/day).

Other approaches for neuropathic pain of any type include a selective serotonin reuptake inhibitor (eg, fluoxetine, paroxetine), an oral local anesthetic (eg, mexiletine beginning at 150 mg/day, then gradually increasing to the usual maximum dose of 300 mg q 8 h), and an alpha$_2$-adrenergic agonist (eg, clonidine beginning at 0.1 mg/day, increased as tolerated). Topical creams, such as the anesthetics 5% lidocaine and EMLA (eutectic mixture of local anesthetics), or topical capsaicin 0.025% or 0.075%, are sometimes tried. Diphenhydramine in relatively high doses (eg, 400 to 600 mg/day po in divided doses) and IV naloxone infusions have been anecdotally reported to be salutary in central pain states. Other drugs for neuropathic pain are sometimes used (see COMPLEX REGIONAL PAIN SYNDROME, below). Although a relationship between analgesic effect and blood levels has not been determined, monitoring blood levels, when possible, may help assess compliance and record an effective baseline level for future reference.

COMPLEX REGIONAL PAIN SYNDROME

(Reflex Sympathetic Dystrophy and Causalgia)

A chronic pain state induced by soft tissue or bone injury (complex regional pain syndrome [CRPS] type I, or reflex sympathetic dystrophy) or by nerve injury (CRPS type II, or causalgia) in which pain is associated with autonomic changes (eg, sweating or vasomotor abnormalities) and/or trophic changes (eg, skin or bone atrophy, hair loss, joint contractures).

Radionuclide bone scan (showing increased uptake), x-rays of the extremity (showing bone loss), and thermography (detecting increased or decreased skin temperature) may be useful in demonstrating autonomic or trophic changes.

The complex regional pain syndrome is more likely to involve sympathetically maintained pain than other types of chronic pain.